REMARKS

Status of the Claims

Claims 1-9 were canceled in the Preliminary Amendment. Claims 34-39 have been withdrawn from the application, as being drawn to a non-elected invention. Claims 10-21 and 24-33 are pending. Claims 22 and 23 are cancelled with this amendment. Claims 21, 25, 31 and 33 are currently amended. Claims 25, 31 and 33 are amended to correct obvious typographical errors.

Rejection Pursuant to 35 U.S.C. § 112, First Paragraph

Reconsideration is requested of the rejection of claims 18-33 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Specifically, the Examiner pointed out that the Applicants had not specified the basis for each and every limitation in claims 18-33 as filed in the Preliminary Amendment, dated October 10, 2001.

Support for each of the limitations specified under (a)-(l) can be found in the application as follows:

(a) The recitation of *"SEQ ID NO:1 from position 59 through position 2204, the construct also including a 5' untranslated sequence located between the eukaryotic promoter and position 59, the 5' untranslated sequence being devoid of a sequence encoding a translational initiation codon, the construct also including a 3' untranslated sequence downstream of position 2204, the 3' untranslated region comprising a eukaryotic polyadenylation sequence, where the host cells are cultured under*

conditions providing for the expression and secretion of the glycoprotein into a culture medium" in claim 21.

Support for this recitation can be found in Example 2 (page 4, lines 37-38 and page 5, lines 1-12) and Figure 1. It is stated in Example 2 that the sequence of Fig. 1 includes the ApaI restriction fragment, 58 base pairs of 5' untranslated sequence (nucleotides 0001-0058), and 222 base pairs of the 3' noncoding DNA sequence. The erythropoietin fragment in Figure 1 includes a total of 2426 base pairs, and knowing that untranslated regions are from nucleotide 1 to nucleotide 58 at the 5' end and the last 222 nucleotides at the 3' end (2205-2426), it can easily be determined that ApaI fragment includes nucleotides 59-2204. Support for "the 5' untranslated sequence being devoid of a sequence encoding a translational initiation codon" can be found in Example 2 (page 5, lines 4-7) and page 2, lines 32-35. Support for "the 3' untranslated region comprising a eukaryotic polyadenylation sequence" can be found in Example 2 (page 5, lines 7-9), page 2, lines 35-37, and Figure 2.

(b) The recitation of *"where the host cells are treated with methotrexate"* in claim 20.

Support for several treatments of host cells with methotrexate can be found in Example 4.

(c) The recitation of *"methotrexate of about 1μM to about 10mM"* in claims 21 and 22.

Applicants note that claim 21 has been amended to recite "methotrexate of about 1μM to about 1mM". Support for this recitation can be found in Example 4 (page 7, lines 25-27).

Claim 22 has been cancelled rendering this rejection moot.

(d) The recitation of *"prior to being treated with a second concentration of methotrexate, the second concentration being lower than the first concentration"* in claim 22.

(e) The recitation of *"methotrexate is about 1 μM to about 1mM"* in claim 23.

Claims 22 and 23 have been canceled, rendering the rejection of claims 22 and 23 moot.

(f) The recitation of *"metallothionein promoter as the eukaryotic promoter operably linked to the insert"* in claim 25.

For support, see Figure 3 depicting plasmid pBD-EP, wherein metallothionein I (MT-I) promoter was operably linked to the insert. Also, see Example 3, page 6, lines 1-5 for MT-I promoter sequence.

(g) The recitation of *"at least two million units of erythropoietin activity per liter of culture medium are obtained, the units of activity being measured by a radioimmune assay using a mammalian erythropoietin as a standard"* in claim 26.

Support for this recitation can be found in the summary of the invention (page 2, lines 7-10) and in Example 5 (page 10, lines 19-25).

(h) The recitation of *"wherein the cells are stably transformed"* in claims 28 and 29.

Support for this recitation can be found in the summary of the invention (page 2, lines 7-9), page 2, lines 24-28, and Example 4 (page 7, lines 11-30).

(i) The recitation of *"glycoprotein is produced at a level of about 500 to about 7000 units per ml of culture medium, the units being determined by an in vitro erythroid*

colony forming bioassay using mouse bone marrow cells and partially purified sheep erythropoietin as a comparative standard" in claim 28.

Support for "glycoprotein is produced at a level of about 500 to about 7000 units per ml of culture medium" can be found in Table 2 and Example 5 (page 9, lines 32-34). Support for "the units being determined by an in vitro erythroid colony forming bioassay using mouse bone marrow cells and partially purified sheep erythropoietin as a comparative standard" can be found in Example 5, page 9, lines 35-38, and page 10, lines 1-2.

(j) The recitation of *"glycoprotein is produced at a level of about 6 to about 85 µg per ml of culture medium"* in claim 29.

For support, see Table 2, under "micrograms protein."

(k) The recitation of "*an adenovirus-2 major late promoter sequence, an adenovirus-2 tripartite leader and third leader 5' splice sequence, an immunoglobulin 3' splice sequence and a late SV-40 polyadenylation signal sequence, the insert being operably linked downstream of the adenovirus-2 major late promoter sequence and upstream of the immunoglobulin 3' splice site to provide for the expression and secretion of the glycoprotein into a culture medium"* in claim 31.

Support for this recitation can be found in Example 3 (page 5, lines 15-37).

(l) The recitation of *"metallothionein promoter operably linked to the insert to provide expression and secretion of a glycoprotein into the culture medium"* in claim 33.

For support, see Figure 3 depicting plasmid pBD-EP, wherein metallothionein I MT-I) promoter was operably linked to the insert. Also, see Example 3, page 6, lines 1-8 and Example 4 (page 7, lines 24-30).

ELX-5795L-6 (BXTD 9006.3)
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Rejection Pursuant to the Doctrine of Obviousness-type Double Patenting

Claims 10-17 and 27-30 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of the U.S. Patent No. 5,688,679 in view of either one of Nimtz *et al.* (*Eur. J. Biochem.* 213:39, 1993) or Yanagi *et al.* (*DNA* 8(6):419, 1989). The Applicants acknowledge the Examiner's remark and submit herewith a terminal disclaimer in accordance with § 1.321(c).

In view of the above, Applicants respectfully request favorable reconsideration and allowance of the pending claims.

The Commissioner is hereby authorized to charge any deficiency or overpayment of the required fee to Deposit Account No. 19-1345.

Respectfully submitted,

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